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Investigation of segmental differences in the gastrointestinal tract of rats

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INTRODUCTION & AIM

Different *in vitro* methods are widely used to predict oral bioavailability of drugs, but to improve the *in vitro in vivo* correlation (IVIVC), it is important that *in vitro* data are generated under conditions as close to the *in vivo* situation as possible. Several simulated gastrointestinal (GI) fluids have been developed to accommodate this need, but they are based on the composition of GI fluids in humans and dogs (1). The aim of the current study was to investigate pH, osmolality, bile acid and phospholipid concentration in different segments of the GI tract in rats, with the overall aim of producing a rat fasted state simulated intestinal fluid (FaSSIF).

METHODS

Six male Sprague Dawley rats weighing approximately 300 g were fasted overnight prior to the experiments. The rats were anesthetized, and the abdomen was opened through the midline. The pH was measured with a micro electrode through a small hole in six different segments of the GI tract; forestomach, glandular stomach, proximal small intestine (5 to 20 cm distal to the stomach), distal small intestine (5 to 20 cm proximal to the caecum), caecum and colon (Fig. 1). Fluid samples were collected from the stomach, proximal and distal small intestine, and the osmolality was measured. The concentration of bile acids and phospholipids were determined using a fluorometric and colorimetric enzymatic assay kit, respectively.

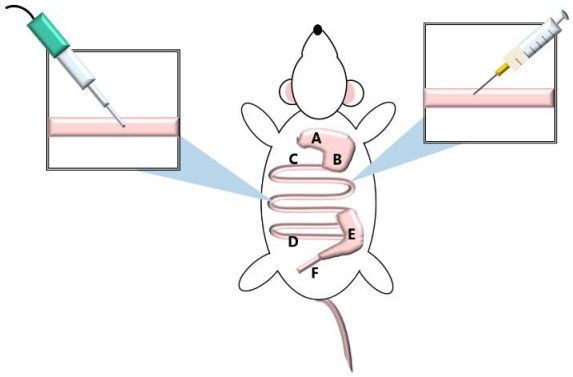

Fig. 1: Schematic of the sampling and pH measurements in the GI tract of a rat in A: Forestomach, B: Glandular stomach, C: Proximal small intestine, D: Distal small intestine, E: Caecum, F: Colon.

RESULTS

The pH was measured in six different segments of the GI tract, and the observed values are shown in Table 1.
In general, it was possible to determine pH with small standard deviations between the rats, however, the standard deviations observed in the stomach were larger than observed for the other segments. The osmolality in the stomach, proximal and distal small intestine was determined to be 237 ± 19, 313 ± 13 and 328 ± 13 mOsm, respectively. Bile acids and phospholipids were hardly detected in the stomach (1.5 ± 0.9 mM and 0.5 ± 0.5 mM, respectively). In the small intestine, the bile acid concentration was determined to be 24.4 ± 10.5 mM in the proximal part and then increased to 46.8 ± 15.2 mM in the distal part. The phospholipid concentration was similarly higher in the proximal part of the small intestine (2.5 ± 1.7 mM) than in the distal part, where it was hardly detected (0.2 ± 0.3 mM).

Table 1: pH values measured in six different segments of the GI tract (mean ± SD, n=4-6).

	Forestomach	Glandular stomach	Proximal small intestine	Distal small intestine	Caecum	Colon
pH	2.0 ± 0.5	2.9 ± 0.7	7.5 ± 0.3	7.8 ± 0.3	7.6 ± 0.2	7.6 ± 0.2

CONCLUSION & FUTURE PERSPECTIVES

Different segments of the rat GI tract were investigated regarding pH, osmolality and bile acid and phospholipid concentration. The obtained data will serve as a valuable platform for development of a rat FaSSIF which may lead towards better IVIVC in the future.

REFERENCES

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